From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

Rec'd PCT/PTC 06 JAN 2005

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *day/month/year*	24 NOV 2004
Applicant's or agent's file reference p21684pcau	**IMPORTANT NOTIFICATION**

International Application No.	International Filing Date	Priority Date
PCT/AU2003/000935	23 July 2003	23 July 2002

Applicant

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translations to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

Name and mailing address of the IPEA/AU	Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	WARREN TAYLOR Telephone No. (02) 6283 2229

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference p21684pcau	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. PCT/AU2003/000935	International Filing Date *(day/month/year)* 23 July 2003	Priority Date *(day/month/year)* 23 July 2002

International Patent Classification (IPC) or national classification and IPC

Int. Cl. [7] C08G 18/32, 18/10, 18/77; C08K 5/00, 3/32; A61L 27/18, 27/58, 31/06

Applicant

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheet(s).

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [ ] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [X] Certain observations on the international application

Date of submission of the demand	Date of completion of the report
28 January 2004	23 November 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **WARREN TAYLOR** Telephone No. (02) 6283 2229

I. Basis of the report

1. With regard to the **elements** of the international application:*

- [ ] the international application as originally filed.
- [X] the description, pages **1-55,** as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [X] the claims, pages **57-60,** as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages **56,** received on **26 August 2004** with the letter of **23 August 2004**
- [X] the drawings, pages **1/18 – 18/18,** as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the sequence listing part of the description:
  pages , as originally filed
  pages , filed with the demand
  pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- [ ] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **8-28**	**YES**
	Claims **1-7**	**NO**
Inventive step (IS)	Claims **8-28**	**YES**
	Claims **1-7**	**NO**
Industrial applicability (IA)	Claims **1-28**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

The present application appears directed to biocompatible, biodegradable polymer compositions capable of in-vivo curing with low-heat generation (as well as ex-vivo curing) to form materials suitable as scaffolds in tissue engineering applications (eg, bone and cartilage repair).

The problem to solve appears to reside in providing biodegradable, biocompatible polymers capable of supporting living and non-living biological additives during preparation and use, which are also flowable and preferably injectable, in tissue engineering applications.

After considering the applicant's submission the following documents from the first and second opinions are considered relevant to the current application;

D1 – EP 0837084 (formerly D4)

D2 – US 6376637 B (formerly D11)

D3 – WO 2002/010247 A (formerly D6)

In response to the applicant's submissions the following comments are made –

The present invention reaction product chemical structure (denoted as structure 2 by the applicant) appears to have more than one urethane/urea linkage where said linkages occur within repeating units. If this feature, which is accepted as being different to the structure inferred by D1 (with regard to urea/urethane linkage frequency only), is an essential feature to the present invention then it should be properly reflected in the independent claims. However, D1 discloses a prepolymer reaction product derived from the reaction of diNCO and multifunctional molecules having at least 2 functional groups. Flowability of the prepolymer can be inferred from the commonplace knowledge of the art stated at p6 (L7) and further at p3 (L30) of D1, which discloses an inherent viscosity of the prepolymer between 0.05-0.5 dL/g. The flowable prepolymers of D1 also appear to encompass 'gel-like' polymers. The applicant's in their submission (p7, L12-29) refer to the terms 'flowable' and 'injectable' as being interchangeable although the current description clearly indicates that the present invention prepolymers are only preferably injectable and therefore not essential to the present invention. Therefore it is not immediately evident why the disclosure of D1 does not deprive present claims 1-2, 4-5 and 7 of novelty in this regard.

It is also unclear why the applicants in their submission refer to diNCO as the reactant with the core molecule defined therein instead of the claimed NCO (present claim 1). If a difference exists between diNCO and NCO reactants, the independent claims should also reflect this aspect. The applicant's submission also frequently discusses the NCO component of the cited art is present as a result of an 'end capping' process and therefore confirming novelty of the current application in light of D1 on this basis. Present claim 1 is a composition claim *per se* and therefore the notion of a sequential order of addition of reactants to the reaction scheme is moot. Subsequently, it is considered that D1 currently anticipates at least present claims 1-2, 4-5 and 7. .

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box V

D2 discloses dendritic/ highly branched PU's. Said PU's are derived from reactions between diNCO's and compounds having at least 2 reactive groups to NCO which form a prepolymer composition prior to PU production. The disclosure of D2 includes Examples 2-4 which are not necessarily solid PU's since the prepolymer product displays turbidity in a suspension. Furthermore, Example 5 utilises substantially the same initial reactants indicated on p13 (glycerol) and p14 (2,4 TDI) of the current application. Hence the reaction product must be liquid or 'flowable'. Whilst the prepolymer of D2 exists – coincident of the present invention claims – it is accepted that D2 does not mention biodegradability of the star polymers. It is considered D2 anticipates at least present claims 1, 2 and 4-5.

D3 discloses a prepolymer forming technique to produce foamed NCO-based polymers by reacting polyol and NCO (especially for PU) thus giving a liquid prepolymer terminated with reactive groups (see p1 – p2, L5). Pages 3-5 of D3 indicate a substantially similar process of prepolymer formation to that of the current application where p9 of D3 provides examples of NCO used and the following page (p10) examples of the active H-containing compounds suitable (includes polyols). The MW range attributed to said H-containing compounds is 200-10000 (p10, L13) and p14 provides examples of the type of dendritic molecule that is also suitable (HBP preferably). It is noted the applicant's response contends the polyols of D3 are not of a 'low MW' suitable for producing injectable, biodegradable polymer compositions, however as mentioned above injectable prepolymers are merely a preferment of the present invention and therefore inessential to the present invention. It is thought the disclosure of D3 provides a highly branched flowable prepolymer with PU/Polyurea linkages as a reaction product derived from NCO and a core molecule having at least 2 functional groups as recited by present claim 1. It is considered D3 anticipates at least present claims 1-6.

NOVELTY (N) Claims 1-7

Independent claim 1 merely defines a star, dendritic or highly branched flowable prepolymer composition, comprised of the reaction product of NCO and a low MW multifunctional core molecule (having at least 2 functional groups), forming urethane/urea groups.

The features, corresponding to at least present claims 1-7 are anticipated and therefore deprived of novelty in light of each of D1-D3 as discussed above.

INVENTIVE STEP (IS) Claims 1-7

Accordingly, since each of D1-D3 deprive at least present claims 1-7 of novelty, these documents are also considered to deprive said claims of an inventive step.

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

1. Page 17 of the description appears to have an inconsistency in the passages covering lines 12-15 of reaction scheme 1. The prepolymer prescribed therein does not appear to have any urethane or urea groups as claimed.

CLAIMS:

1. A star, dendrimer or hyper-branched flowable prepolymer composition comprising the reaction product of isocyanate and low molecular weight multifunctional core molecules having at least two and preferably three or more functional groups that react with said isocyanate to form urethane or urea groups.

2. A prepolymer composition as claimed in claim 1 wherein said low molecular weight multifunctional core molecule is selected from the group consisting of diols, triols, and polyols such as sugar molecules.

3. A prepolymer composition as claimed in claim 1 or 2 wherein said low molecular weight core molecule has a molecular weight of 400 or less.

4. A prepolymer composition as claimed in any one of claims 1-3 wherein said isocyanate is optionally substituted aliphatic, aromatic and hindered isocyanate.

5. A prepolymer composition as claimed in any one of claims 1-4 wherein said isocyanates are aliphatic and asymmetric in molecular shape.

6. A prepolymer composition as claimed in any one of claims 1-5 wherein the viscosity of the prepolymer composition on preparation is about 15,000-200,000 cSt at room temperature.

7. A prepolymer composition as claimed in any one of claims 1-6 further comprising biological and inorganic components selected from the group consisting of cells, progenitor cells, growth factors, other components for supporting cell growth, calcium phosphate, hydroxyapatite, adhesives including fibrin, collagen and transglutaminase systems, surfactants including siloxane surfactants, porogens including silica particles, powdered silica, sugars and sodium chloride type salts, polymeric hollow fibres and gelatin beads